## CONCLUSIONS

1. Unsuspected urinary tract infections were discovered in 4.4 per cent of a selected group of relatively healthy young women attending the Out-Patient Clinic of Stanford University Hospital.

2. The cases of five patients with definite infection, including three with chronic active pyelonephritis, are presented in detail and the response to treatment is outlined.

3. The sequelae of infections of the urinary tract are discussed and a plea is made for more frequent and detailed study of the urine by clinicians.

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# Treatment of Urinary Tract Infections

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IN the treatment of urinary tract infections, the urologist, when this is feasible, should assume the management and responsibility for proper care. He is equipped both with experience and facilities to do so. With the advent of the sulfonamides and antibiotics, and their universal use, fundamental facts are lost sight of and unnecessary complications ensue. Enumeration of these facts may seem elementary but their application will save much time and misery for the patient.

## ETIOLOGY

These infections are the result of invasion of the urinary tract by organisms causing various inflammatory changes. There are only a few kinds of such organisms, and they are classified as (1) pyogenic (coccus and bacillus), and (2) non-pyogenic or specific (gonococcus and tubercle bacillus). The infection may be a mixed one. This discussion is limited to the pyogenic form. Because of the predilection of each form for different parts of the tract, this differentiation is essential to successful treatment.

## DIAGNOSIS

Uncomplicated acute urinary tract infection usually is self-limited and clinically disappears in two to four weeks. Acute appendicitis, cholecystitis, and salpingitis may simulate it, and early establishment of the correct diagnosis then may be life-saving. The subacute and chronic forms are easily diagnosed but the damage may have been done. The focal renal infections, such as infected infarcts, multiple abscess, or carbuncle may go undiagnosed or extend to the perirenal area and require surgical operation for relief. Such infections are usually coccal in origin. Thus, fundamentals are of value. These include taking a careful history, general examination, examination of the genitalia, microscopic examination of the urine for pus and for organisms with or without pus (cocci or bacilli) or pus with tubercle bacilli, examination of the prostate and seminal vesicles, roentgenographic examination of the whole tract including the prostate, and, last but very important, determination of kidney function.

Naturally, these are not done in a patient with pyuria due to a urethral discharge alone, but unless the genitalia are examined before the patient voids, the discharge may not be seen.

In treating patients with acute infection or those with recurrence or chronic infection, this data will prove valuable and its recording will gain the confidence of the patient. The general practitioner can make the examinations but may require assistance in interpretation and advice as to instrumentation.

*Collection of Urine:* This must be properly done. In the female, the specimen should be taken by catheter after thorough cleansing of the external

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Read before the Section on General Practice at the 76th Annual Session of the California Medical Association in Los Angeles, April 30-May 3, 1947.

genitalia. In the male, a catheter is not necessary when the patient can void, but the genitalia should be thoroughly cleansed. In each case any discharge of pus or blood should be stained and examined microscopically. This alone may lead to the diagnosis. The next step in the male is to have him void in a steady stream and catch some of the urine in two or three glasses, the second of which should be sterile. This is a true bladder specimen and will suffice for cultural and microscopical studies.

Examination of the urine should include a Gram-stain or a simple methylene blue smear. Cocci or bacilli or both may be noted and proper treatment instituted while a report on culture growth is awaited. Tubercle bacilli should be looked for.

It is very important to make blood cultures in cases of acute infection. These are commonly positive but not necessarily ominous. Fortunately, the bacillus is the most common invader as well as the least serious, as the infection then usually involves only the drainage system of the tract, while the coccus is apt to involve the deeper structures of the kidney such as the parenchyma only, and thus its presence may present no signs or symptoms in the urine. Negative findings in the urine in such cases may hinder early diagnosis, so that surgical operation becomes necessary to save life. In a generalized septicemia, both kidneys become involved.

Blood chemical determinations also are advisable at times.

Predisposing factors to infection are mainly stasis and obstruction. These lead to recurrences, chronicity, and more or less damage. Again, the urologist enters with his equipment, to determine whether complications exist, as a successful treatment presupposes their eradication.

At times, infection with obstruction requires immediate instrumentation. This is justified and advisable, provided drainage is also secured. The obstruction can thus be localized and the extent of damage both by infection and back pressure determined.

Intravenous urograms are useful, but are not advisable in the presence of high fever. Too much reliance should not be placed on their interpretation. They are of value mainly to determine the presence or absence of anomalies, hydronephrosis, or obstruction. In the subacute, chronic, and recurring infections, thorough instrumental examination must be made, including relative functional tests and bilateral pyelo-ureterograms.

## TREATMENT

Consideration of treatment calls to mind certain fundamental questions: (1) Is the infection acute or chronic or recurrent? (2) Is the invader coccal, bacillary, or specific? (3) Is a complication present (stone, obstruction, or anomaly), or the tract normal? (4) Is it an upper, lower, or combined tract involvement and is it unilateral or bilateral? (5) Is there loss of renal function? These questions the urologist can answer.

Some simple cases of pyuria with only local bladder symptoms respond readily to prostatic massage and urethro-vesical irrigations with or without chemotherapy. Again, in females, simple bladder lavage through a catheter may suffice. Acute and toxic infections demand early treatment for symptomatic relief and the prevention of complications.

Drugs alone seldom cure. They are mainly prophylactive and palliative. Undoubtedly, with our present-day knowledge of their uses and actions, much less urinary tract diseases will develop. However, indiscriminate use of them is to be condemned as the patient may be rendered symptom-free, with the clearing of local infection, although the underlying disease persists and may progress. Only a few medicines are good. To use them empirically is unadvisable. Too often the subsidence of sypmtoms is interpreted as a cure. In many cases, bacteriuria is symptomless but chronic. With a recurrence, the patient may drift or seek drug-store advice, and much early time is lost in making an accurate diagnosis.

*Water* is still a medicine of choice. The drinking of three to four liters daily is usually advisable. Preliminary studies should have ascertained if this amount is safe.

*Diets* are difficult to administer as well as to tolerate.

## DRUGS

The drugs useful in treatment are acidifiers, sulfonamides, arsenicals, and antibiotic. The dyes probably have some psychic effect. Methylene blue, .065 gm. two to three time daily, does decrease bladder discomfort. Alkalies and bladder sedatives are palliative, as are copious fluids. Mandelic acid is a valuable acidifier; in divided doses (8 to 10 gm. daily), it will cause the pH to reach 5.5 where it may be bacteriostatic. The disadvantages are that the urine must be concentrated, which means a low fiuid intake. Furthermore, impaired kidney function contraindicates its use. It may be of value against Gram-negative bacilli or streptococcus fecalis.

*Sulfonamides:* The results with these are very satisfactory. The author feels they are the drugs of choice if tolerated, and if the patient can be observed. Small doses of 1 to 2 gm. daily, and at times even less, are just as efficacious as around-the-clock medication, and the likelihood of intolerance is less. They can be used where renal function is impaired. With the small amounts advocated, blood level studies are not necessary. As these drugs are eliminated almost entirely by the kidneys, it is not necessary to concentrate the urine, and fluids can be forced. Mild signs of toxic reaction such as headache, dizziness, or weakness, which are common, should not be a reason for discontinuance. Careful clinical observation will usually give sufficient and ample warning. There is one reaction from sulfonamides which is common and often deceptive. This is the persistence of fever or spiking temperatures even with such small amounts as 0.5 gm. a day. When fever is due to the drug, it is out of proportion to clinical findings (such as pain, tenderness, masses)

or urinary findings. If the drug is the cause of fever, stopping it reduces the temperature in 24 to 36 hours.

The author believes sulfathiazole is as good as any of the sulfonamides. It has less tendency to crystal formation in the urine than sulfadiazine, although this tendency in sulfadiazine in 0.5 to 2 gm. doses daily with copious fluids and with sodium bicarbonate, if desirable, does not present too great a complication. If neither sulfathiazole nor sulfadiazine is tolerated, switching to others of the group is indicated, not forgetting sulfanilamide, again in amounts of 0.3 to 1 gm. daily. Pyuria may persist despite the giving of sulfa drugs, however, which may mean that the organisms are resistant or that a secondary infection, possibly one that has been kept in check by the more virulent organism, has arisen. Sulfonamides seem to be most effective against most Gram-negative organisms and some Gram-positive cocci, but are not effective against streptococcus fecalis.

*Arsenicals:* One overlooked agent is neoarsphenamine. In pyuria caused by cocci, such as staphylococci, or in a bacterial pyuria, it may be specific. Such low-grade pyurias caused by kidney infection usually clear up with three injections of 0.6 gm. given at five-day intervals.

*Penicillin* is less effective than the sulfa compounds in the usual run of urinary tract infections. Because of its rapid elimination, the body must be kept saturated either by around-the-clock injections or by single large doses. However, for coccal infections, or where the process has involved the kidney parenchyma, as in multiple abscess or carbuncle, or for infections in the perirenal area, penicillin is definitely indicated. Its good effects in some bacillary infections may be due to the atypical sensitivity of the organisms. Where the possibility of a secondary invader exists or an inhibited organism flares up, the good results from penicillin when the sulfa drugs have failed warrant its use either with the sulfonamides or later. Penicillin and a sulfa drug are advisable as a prophylaxis following catheterization or cystoscopy or surgical operation to prevent unfortunate and prolonged sequellae.

*Streptomycin* is not a cure-all but is often effective where all other drugs fail. However, besides its high cost and the small supply, there are other objections to use of the drug. Its use is inadvisable if kidney function is impaired, as 80 per cent of it is excreted through the kidneys if it is injected perenterally; it reaches a high degree of concentration in the urine in less than eight hours. It is of no value where stasis exists. Organisms killed by it in vitro are not necessarily affected in the body. Tolerance is often built up so that large divided doses must be used at the outset, at least 3 gm. daily. If taken orally, 90 per cent of the drug is not absorbed.

## SURGICAL TREATMENT

Treatment by medication is not always successful. Ten to 30 per cent of patients have recurrences, and major surgical operation is necessary in probably about 30 per cent. With stones complicating, fully 50 per cent require nephrectomy. About 25 per cent of patients with simple pyelonephritis have a recurrence of the disease, with the opposite kidney affected in some cases. There is permanent kidney damage, as shown by functional tests, in about 30 per cent of patients who have had simple pyelonephritis.

## CONCLUSION

The urogolist should manage the treatment of urinary tract infections. He can make an accurate diagnosis, outline the treatment, medical or surgical, and handle complications.

Complications are factors predisposing to chronicity and recurrences.

The organism causing the infection should be identified. A predilection for different parts of the tract may be demonstrated.

Only a few drugs are of value. The sulfonamides are the drugs of choice. Penicillin and streptomycin are good adjuncts but have limitations.

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